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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/522,356	01/26/2005	Christopher Bruce Alexander Whitelaw	102286.155US1	1380

23483 7590 08/13/2008

WILMERHALE/BOSTON
60 STATE STREET
BOSTON, MA 02109

EXAMINER	
CHEN, SHIN LIN	

ART UNIT	PAPER NUMBER
1632	

NOTIFICATION DATE	DELIVERY MODE
08/13/2008	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

michael.mathewson@wilmerhale.com
teresa.carvalho@wilmerhale.com
sharon.matthews@wilmerhale.com

Office Action Summary	Application No.	Applicant(s)	
	10/522,356	WHITELAW ET AL.	
	Examiner	Art Unit	
	Shin-Lin Chen	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 May 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *22-28 and 30-35* is/are pending in the application.

4a) Of the above claim(s) *34 and 35* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *22-28 and 30-33* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicants' amendment and declaration by Dr. Whitelaw filed 5-14-08 have been entered. Claims 22-25, 28, 30 and 33-35 have been amended. Claim 29 has been canceled. Claims 22-28 and 30-35 are pending.

It should be noted that Applicants elect species A, claims 22-33, for examination in the "Response to Further Restriction Requirement" filed 11-21-07. Therefore, claims 34 and 35 have NOT been and will NOT be examined. It is noted that Applicants elected beta-lactoglobulin as lipocalin species, epitope species of SEQ ID No. 1, which is EQKLISEEDL from c-myc, and promoter element Cyp1a1 in the response filed on 5-29-07. Claims 22-28 and 30-33 are under consideration.

Specification

1. The disclosure remains objected to because it contains an embedded hyperlink and/or other form of browser-executable code, for example, pages 8 and 16. Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01.

Applicants argue that applicants are not attempting to incorporate the contents of the sites to which the links are directed to and the hyperlinks are part of the written description (amendment, p. 10). This is not found persuasive because:

When a patent application with embedded hyperlinks and/or other forms of browser-executable code issues as a patent (or is published as a patent application publication) and the patent document is placed on the USPTO web page, when the patent document is retrieved and viewed via a web browser, the URL is interpreted as a valid HTML code and it becomes a live web link. When a user clicks on the link with a mouse, the user will be transferred to

another web page identified by the URL, if it exists, which could be a commercial web site. USPTO policy does not permit the USPTO to link to any commercial sites since the USPTO exercises no control over the organization, views or accuracy of the information contained on these outside sites. If hyperlinks and/or other forms of browser-executable code are embedded in the text of the patent application, examiners should object to the specification and indicate to applicants that the embedded hyperlinks and/or other forms of browser-executable code are impermissible and require deletion. (MPEP 608.01 VII, 37 CFR 1.57(d)).

If applicants are not attempting to incorporate the contents of the sites to which the links are directed to, it is imperative that the hyperlinks and/or other form of browser-executable code be deleted from the specification.

Claim Rejections - 35 USC § 112

2. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3. Claims 22-28 and 30-33 remain rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention and is repeated for the reasons set forth in the preceding Official action mailed 12-14-07. Applicant's arguments filed 5-14-08 have been fully considered but they are not persuasive.

Applicants cite Dr. Whitelaw's declaration and argue that the claims have been amended to recite "transgenic rodent" which encompass much fewer animals than "transgenic non-human

animal", and the specification provides sufficient information to one skilled artisan to produce a transgenic rodent. Example 11 teaches several methods to produce transgenic animal, including pronuclear injection, blastocyst injection of transfected cells and using viral vectors, and these methods were well known in the art. Applicants further argue that preparation of transgenes containing the Cyp1a1 promoter driving expression of myc epitope tagged BLG reporter was known in the art, and methods of detecting and screening for a gene activation event of toxicologically induced stress were also known in the art at the time of the invention (amendment, p. 12-14). This is not found persuasive because of the reasons set forth in the preceding Official action mailed 12-14-07. It is noted that forty percent of mammal species are rodents, and they are found in vast numbers on all continents other than Antarctica. Common rodents include mice, rats, squirrels, chipmunks, gophers, porcupines, beavers, hamsters, gerbils, guinea pigs and degus. There are over 2000 species of rodent. Therefore, "transgenic rodent" still encompass numerous different transgenic animals. Although methods of making transgenic animals were known in the art, however, the state of the art of transgenics held that the resulting phenotype of a transgenic animal was unpredictable at the time of the invention. The specification fails to disclose any transgenic rodent having any particular phenotype and said transgenic rodent can be used for detecting and screening the claimed gene activation event. The specification fails to disclose the structural feature or phenotype of the claimed various transgenic rodents. The structural features and phenotypes of the transgenic rodents that can distinguish said transgenic rodents from wild-type rodents have not been disclosed. Although it was known how to detect gene expression or protein expression, however, since the resulting phenotype of a transgenic rodent was unpredictable at the time of the invention, therefore,

whether the claimed transgenic rodent would express the peptide tagged BLG reporter and what cell or tissue would express said peptide tagged BLG reporter was unpredictable. It is apparent that applicants do NOT have possession of the various transgenic rodents. Thus, it is concluded that the written description requirement is not satisfied for the transgenic rodents and their uses as claimed.

4. Claims 22-28 and 30-33 remain rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention and is repeated for the reasons set forth in the preceding Official action mailed 12-14-07. Applicant's arguments filed 5-14-08 have been fully considered but they are not persuasive.

Applicants cite Dr. Whitelaw's declaration and argue that the claims have been amended to recite "transgenic rodent" which encompass much fewer animals than "transgenic non-human animal", and the specification provides sufficient information to one skilled artisan to produce a transgenic rodent. Example 11 teaches several methods to produce transgenic animal, including pronuclear injection, blastocyst injection of transfected cells and using viral vectors, and these methods were well known in the art. Applicants further argue that preparation of transgenes containing the Cyp1a1 promoter driving expression of myc epitope tagged BLG reporter was known in the art, and methods of detecting and screening for a gene activation event of toxicologically induced stress were also known in the art at the time of the invention. The art at the time was sufficiently advanced to allow for making amino acid deletions, assaying for

protein activity, and picking the protein with activity without undue experimentation (amendment, p. 14-17). This is not found persuasive because of the reasons set forth in the preceding Official action mailed 12-14-07 and the reasons set forth above. It is noted that forty percent of mammal species are rodents, and they are found in vast numbers on all continents other than Antarctica. Common rodents include mice, rats, squirrels, chipmunks, gophers, porcupines, beavers, hamsters, gerbils, guinea pigs and degus. There are over 2000 species of rodent. Therefore, "transgenic rodent" still encompass numerous different transgenic animals. Although methods of making transgenic animals were known in the art, however, the state of the art of transgenics held that the resulting phenotype of a transgenic animal was unpredictable at the time of the invention. The specification fails to disclose any transgenic rodent having any particular phenotype and said transgenic rodent can be used for detecting and screening the claimed gene activation event. The specification fails to disclose the structural feature or phenotype of the claimed various transgenic rodents. The structural features and phenotypes of the transgenic rodents that can distinguish said transgenic rodents from wild-type rodents have not been disclosed. Although it was known how to detect gene expression or protein expression, however, since the resulting phenotype of a transgenic rodent was unpredictable at the time of the invention, therefore, whether the claimed transgenic rodent would express the peptide tagged BLG reporter and what cell or tissue would express said peptide tagged BLG reporter was unpredictable at the time of the invention.

Further, the specification contemplates using blastocyst injection of transfected cells to generate transgenic non-human animals. It appears that only two mouse ES cell lines can be used to generate transgenic mice and no other known ES cell lines have been established to

generate any other transgenic animals at the time of the invention. The biological function of protein was unpredictable from mere amino acid sequence at the time of the invention and different beta-lactoglobulin could have different biological functions, which adds to the unpredictable resulting phenotype of the transgenic rodents expressing various beta-lactoglobulin proteins.

In view of the reasons set forth above, one skilled in the art at the time of the invention would not know how to use the claimed transgenic rodent for the claimed method. One skilled in the art at the time of the invention would require undue experimentation to practice over the full scope of the invention claimed. The claims remain rejected for the reasons of record.

Conclusion

No claim is allowed.

5. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event,

however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shin-Lin Chen whose telephone number is (571) 272-0726. The examiner can normally be reached on Monday to Friday from 9:30 am to 6 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Peter Paras can be reached on (571) 272-4517. The fax phone number for this group is (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

Shin-Lin Chen, Ph.D.
/Shin-Lin Chen/

Primary Examiner, Art Unit 1632